NDA 50-588/S-026 AUG 05 1999

Zeneca Pharmaceuticals
Attention:Gerald L. Limp
Manager, Marketed Products Group
1800 Concord Pike
P.O. Box 15437
Wilmington, DE 19850-5437

Dear Mr. Limp:

Please refer to your supplemental new drug application dated May 1, 1997, received May 6, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cefotan® (cefotetan disodium for injection). We note that this application is subject to the exemption provisions contained in section 125(d)(2) of Title I of the FDA Modernization Act of 1997.

Reference is also made to the Agency's approvable letter dated December 16, 1998.

We acknowledge receipt of your submissions dated May 9, 1997, and April 15, 1999. Your submission of April 15, 1999 constituted a complete response to our December 16, 1998 action letter.

We note that this supplement was submitted as a 'Special Supplement - Changes Being Effected' under 21 CFR 314.70(c).

This supplemental new drug application provides for the following changes to the label:

1. A revised CONTRAINDICATIONS section which reads:

   "Cefotan is contraindicated in patients with a known allergy to the cephalosporin group of antibiotics and in those individuals who have experienced a cephalosporin associated hemolytic anemia."

2. The addition of the two following capitalized paragraphs in the WARNINGS section that strengthen the warning for hemolytic anemia:

   "AN IMMUNE MEDIATED HEMOLYTIC ANEMIA HAS BEEN OBSERVED IN PATIENTS RECEIVING CEPHALOSPORIN CLASS ANTIBIOTICS. SEVERE CASES OF HEMOLYTIC ANEMIA, INCLUDING FATALITIES, HAVE BEEN REPORTED IN ASSOCIATION WITH THE ADMINISTRATION OF CEFOTETAN. SUCH REPORTS ARE UNCOMMON. IF A PATIENT DEVELOPS ANEMIA ANYTIME WITHIN 2-3 WEEKS SUBSEQUENT TO THE ADMINISTRATION OF CEFOTETAN, THE DIAGNOSIS OF A CEPHALOSPORIN ASSOCIATED ANEMIA SHOULD BE CONSIDERED AND THE DRUG STOPPED UNTIL THE ETIOLOGY IS DETERMINED WITH CERTAINTY. BLOOD TRANSFUSIONS MAY BE CONSIDERED AS NEEDED."

   "PATIENTS WHO RECEIVE PROLONGED COURSES OF CEFOTETAN FOR TREATMENT OF INFECTIONS SHOULD HAVE PERIODIC MONITORING

FOR SIGNS AND SYMPTOMS OF HEMOLYTIC ANEMIA INCLUDING A MEASUREMENT OF HEMATOLOGICAL PARAMETERS WHERE APPROPRIATE."

Your submission date of April 15, 1999 is the implementation date for this change.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the submitted final printed labeling (package insert submitted Final Printed Labeling). Accordingly, the supplemental application noted above is approved effective on the date of this letter.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact Mr. R. Grant Hills, Project Manager, at (301) 827-2125.

Sincerely,

Gary K. Chikami, M.D.
Director
Division of Anti-Infective Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research